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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/869,049	06/22/2001	Yasuki Kato	506.40278X00	1134

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EXAMINER
SRIVASTAVA, KAILASH C

ART UNIT	PAPER NUMBER
1651	10

DATE MAILED: 10/10/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/869,049	KATO ET AL.	
	Examiner	Art Unit	
	DR. Kailash C. Srivastava	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03/14/2002 (Paper Number 7)* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-30* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *5 and 9* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. The assigned Examiner to your application in the USPTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Examiner Kailash C. Srivastava in Art Unit 1651.

2. Applicants' Preliminary amendment filed 08/15/2001 as Paper Number 4 is acknowledged and entered.

3. Applicants' amendment filed 03/14/2002 as paper Number 7 is acknowledged and entered. The text of those sections of Title 35 U.S. Code not included in this action can be found in a prior Office action.

4. Applicants' Declaration filed 03/14/2002(Paper Number 8) is acknowledged and entered. However, with this declaration applicants should clearly indicate the purpose of filing the said declaration and appropriate section under which the said Declaration is filed.

5. Claims 9-30 have been added.

6. Claims 1-30 are pending and are examined on merits.

Objection to Information Disclosure Statement

7. The information disclosure statement filed 08/15/2001 as Paper Number 5 is deficient because in this Information Disclosure Statement, the Japanese Patents are not listed under the heading of Foreign Patent Documents. The Examiner has considered this Information Disclosure Statement, however, a revised Information Disclosure Statement with appropriate corrections should be submitted. The Information Disclosure Statement filed 06/03/2002 as paper number 9 is defective because in this document, applicants have not provided a list of the documents that they want the Examiner to consider. Appropriate correction is requested.

Claim Rejections - 35 U.S.C. § 112

8. Claims 1-30 are rejected under 35 U.S.C.§ 112, first paragraph, because the specification, while being enabling for peptides, proteins, enzymes and amino acid derivatives, does not reasonably provide enablement for all the compounds having a free amino group. The specification does not enable any person skilled in the art to which it

pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims. While the specification specifically enables insulin, Enkephalin, doxorubicin hydrochloride and other peptides, to claim all compounds having a free amino group is to claim too broad coverage for applicants' invention.

Applicants' arguments regarding the rejections to Claims 1-8 under 35 U.S.C.§ 112, first paragraph in the Office Action dated 09/14/2001 (paper Number 3) have been fully considered but are not deemed persuasive. Applicants argue that the specification is fully enabled for any compound having a free amino group because the specification recites no restrictions for the compound with free amino group. Applicants further argue that they have conducted experiments with two distinct compounds and in each case the results indicate that their inventive concept is applicable. However, based upon the teachings provided by the instant specification, the specification is still deemed enabled for only insulin, Enkephalin, doxorubicin hydrochloride and peptides, but not for all other compounds that contain free amino group as discussed in the previous Office action.

9. Following is a quotation of the second paragraph of 35 U.S.C. § 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

10. Claims 2 and 5-30 are rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

- The phrase "modified with or included in" renders Claims 5 and 9 vague, unclear and confusing. Applicants should clarify whether this term is open, like the conventional term "comprising", or what does this term define? The Examiner suggests that the applicants should replace this phrase with the transitional phrase "further comprising".

Claim Rejections Under 35 U.S.C. § 102(b)

11. Claims 1-4 stand rejected under 35 U.S.C.§ 102(b) as anticipated by Katsukiyo (JP-07-061999) for the reasons set forth in the Office Action dated 09/14/2001 (paper Number 3).

Applicant's arguments regarding the rejection to claims 1-4 under 35 U.S.C.§ 102(b) as anticipated by Katsukiyo (JP-07-061999) on page 3 of the Office Action dated

09/14/2001 (paper Number 3) have been fully considered but are not persuasive. Applicants argue that the Examiner's cited reference (i.e., Katsukiyo, JP-07-061999) does not anticipate applicants' invention because Examiner's cited prior art reference indicates a protein having an amide bond and the said amide bond "does not rapidly cleave to release a compound having a free amino group in response to changes in pH". However, Claims 1-4 remain anticipated by Katsukiyo (JP-07-061999) for the reasons of record on page 3 of the Office Action dated 09/14/2001 (paper Number 3) and because of the fact that the bond that the applicants have referred to as amide bond (i.e., -CO-NH-) is indeed a peptide bond formed by the union of a carboxylic group of an amino acid with the amino group of another amino acid (See, Stedman's Medical Dictionary, Page 1223, Column 1, Lines 61-64).

Claim Rejections Under 35 U.S.C. § 103(a)

12. Claims 1-30 are rejected under 35 U.S.C. § 103 (a) as obvious over Takenaga et al (US 5,723, 121) in view of Katsukiyo (JP-07-061999) and Masashi et al (JP 9-263579).

Claims recite a pharmaceutical composition comprising a compound obtained through reacting a compound with a free amino group with a reducing sugar wherein the resultant compound is modified with or embedded in a pharmaceutical carrier and upon changes in pH conditions, the said compound with free amino group is released. The said compound with free amino group is insulin or another peptide. The said pharmaceutical carrier may be anyone among: liposome, lipid emulsion, microemulsion, polymer micelle, microcapsule, microspheres and magnetic particles.

Takenaga et al disclose modifying interferon-α (Column 8, Lines 50 to 67) by reacting the said interferon with a solution of lactose lactone in sodium dodecyl sulphate (i.e., sodium lauryl sulphate or SDS) and preparing a pharmaceutical preparation by combining the resultant chemical compound (modified interferon-α) with albumin (Column 9, Lines 1-13). The data on concentration of modified interferon-α accumulation in the liver indicates far higher concentration of modified interferon than unmodified interferon, i.e., control (Column 8, Lines 25-49). Please note that the prior art composition (the disclosed modified interferon-α) intrinsically must function as claimed because the said prior art composition is comprised of same components (i.e., a compound having a free amino group modified with a reducing sugar) as the claimed composition (See e.g., In re Best, 195 USPQ 430, 433-CCPA 1977) as is evidenced by higher accumulation of modified interferon-α in the liver upon administration of interferon-α reducing sugar complex.

Takenaga et al., however, do not disclose insulin to be the peptide with free amino group. They also do not clearly disclose a pharmaceutical carrier (e.g., liposome, lipid emulsion, microemulsion, polymer micelle, microcapsule, microsphere or magnetic particles).

Katsukiyo discloses a sugar-modified protein wherein lactose lactone is reacted with a protein, the said protein being insulin, to make a protein reducing sugar complex (Paragraph 17, Lines 1-6). Since Katsukiyo et al disclose a similar product prepared in the manner instantly disclosed, the product would intrinsically function in the same, or essentially the same manner as in the claimed invention. Therefore, the product disclosed in the prior at reference would intrinsically free the compound with free amino acid group (i.e., insulin) upon changes in the pH.

Katsukiyo, however, does not disclose that the protein-reducing sugar complex resulting from reacting insulin (i.e., a peptide with a free amino group) with a reducing sugar is embedded in an emulsion, microglobule, ribosome or other pharmaceutical carrier.

Masashi et al., teach medications made from enclosing a drug made from protein inserted into a microglobule, ribosome, emulsion or other carrier (e.g., Claims 6 and 12).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the composition and method of Takenaga et al., according to the beneficial teachings of Katsukiyo and Masashi et al., because both Takenaga et al., and Katsukiyo teach modifying a compound with free amino group with a reducing sugar wherein upon changes in the pH conditions, the compound with free amino group is released and Masashi et al., beneficially teach making a drug by inserting a protein into microglobule, ribosome, emulsion or other carrier. Thus, Masashi et al., resolve the deficiency in the teachings of Takenaga et al., and Katsukiyo.

Since each one of the cited prior art references teach a composition comprising ingredients that are common to each one of the compositions (e.g., a protein/ drug), an artisan of ordinary skill would be motivated to combine the teachings from each one of the cited references to obtain a pharmaceutical composition comprising a compound with free amino group modified with a reducing sugar and inserting the resultant compound in a pharmaceutical carrier, wherein said free amino group containing compound is released upon changes in pH. The adjustment of particular conventional working conditions (e.g., the

protein, peptide or the compound containing fee amino group, reducing sugar and the pharmaceutical carrier) is deemed merely a matter of judicious selection and routine optimization, which is well within the purview of the skilled artisan.

From the teachings of the references cited *supra*, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Applicants' arguments regarding the rejections to Claims 1- 8 under 35 U.S.C.§103(a) in Office Action dated 09/14/2001 (paper Number 3) have been considered but are moot in view of the new ground(s) of rejection discussed *supra*.

CONCLUSION

13. No Claims are allowed.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner Kailash C. Srivastava whose telephone number is (703) 605-1196. The examiner can normally be reached on Monday-Thursday from 7:30A.M. to 6:00 P. M. (Eastern Standard or Daylight Saving time).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn, can be reached on (703) 308-4743 Monday through Thursday. The fax phone number for the organization where this application or proceeding is assigned is (703) 305-3014.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Kailash C. Srivastava, Ph.D.
Patent Examiner
Art Unit 1651
(703) 605-1196

October 9, 2002

CHRISTOPHER R. TATE
PRIMARY EXAMINER